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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,331	02/22/2007	Adrienne S. Gordon	27432-16428	2103

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EXAMINER	
CORNET, JEAN P	
ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
01/31/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTOC@Fenwick.com

Office Action Summary	Application No.	Applicant(s)	
	10/550,331	GORDON ET AL.	
	Examiner	Art Unit	
	JEAN CORNET	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,146,148-153 and 155-166* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,146,148-153 and 155-166* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/16/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

. The amendment filed 11/10/2010 in response to the Non-Final office Action of 5/11/2010 is acknowledged and has been entered.

Claims 2-145, 147, 154 are canceled. Claims 1, 146, 148-153, 155-166 are pending and are under current examination.

Information Disclosure Statement

The references cited in the IDS filed on 11/16/2010 have been considered.

Response to Arguments-Claim Rejections - 35 USC § 112

Applicant's arguments with respect to 35 USC § 112 have been fully considered and are persuasive. The rejection of claims 1 and 146 has been withdrawn due to claim amendment.

Response to Arguments-Double Patenting

Applicant's arguments with respect to Double Patenting rejection have been fully considered and are persuasive. The rejection of claims 1, 155, 156, 158, 161-164 has been withdrawn because the copending claims have been amended where the subject matter of this application no longer applies.

Claim Rejections - 35 USC § 103 necessitated by amendment:

Applicant's arguments with respect to 35 USC § 103 have been fully considered and are not persuasive:

Claims 1, 146, 148-153, 155-166 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Diamond et al* **(US5,069,895) cited in IDS in view of** *Dar* **"Modulation of ethanol-induced motor in coordination by mouse striatal A_1 adenosinergic receptor", Brain Research Bulletin, Vol. 55, No. 4, pp 513-520, 2001 and** *Beasley et al* **(US6,159,963) cited in IDS. This rejection is modified to address the new "wherein limitation" and newly added claims 165 and 166.**

The additional comments added to this rejection are necessitated by the claim amendment.

Diamond teaches **methods of treating acute, chronic ethanol** dependence or withdrawal syndrome **by administration of adenosine receptor antagonist to a host in an amount sufficient to reduce the symptoms of ethanol withdrawal** (see claim 1 and 11). Although the standard therapeutically effective dosage for use is generally in the range from about 0.01ug/kg to 5 mg/kg as to claim 150, the amount will depend on the subject being treated, the severity and nature of the affliction, the manner of administration, the potency and pharmacodynamics of the particular agent (col. 5, ln. 11-19). The preferred adenosine antagonist is **PD115199** (col. 3, lines 7-30). Lastly Diamond teaches the administration can be in a single unit dose (col. 4, lines 19-25). PD1151199 is an adenosine receptor subtype A2 as evidenced by claim 158.

Diamond does not expressly teach administration of a dopamine receptor antagonist to treat ethanol addictive behavior.

Dar teaches that striatum is an additional brain motor area involved in mediating ethanol's motor coordination and even the smallest dose of adenosine antagonist significantly attenuated ethanol-induced motor incoordination (page 518, right col). Dar further teaches A_{2A} receptors are mainly localized on the intrinsic striatal neurons and dopaminergic terminals (page 518, left col.).

Beasley teaches **a method for treating substance abuse comprising administering an effective amount of olanzapine (a dopamine antagonist)** to a patient in need thereof (abstract) and a method for treating adverse withdrawal syndrome **said substance abuse include** opiods, cocaine, anxiolytic and hypnotic drugs, and **alcohol** (col. 1, lines 65-67; col, 2, lines 1-3) and adverse withdrawal syndrome refers to an adverse condition resulting form the cessation or withdrawal from substance abuse (col. 5, lines 25-28). For the treatment of alcohol abuse, a lower dosage may be appropriate than treatment than the preferred standard effective dose of 1mg to 25mg per day (col 7, lines 35-45). Olanzapine is a dopamine receptor antagonist D2 as evidenced by claim 155.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to administer an adenosine antagonist with an dopamine antagonist sequentially or simultaneously recited in claims 160 and 161 to mitigate one or more symptoms associated with chronic consumption of a substance abuse by administration of adenosine receptor antagonist and dopamine receptor antagonist.

One skill in the art would have been motivated to administer the combined D2 and A2 antagonists to mitigate one or more symptoms associated with chronic consumption of alcohol because each of the therapeutics agents with an effective dose had been individually taught in the prior art to be successful at treating substance abuse. The instant situation is amenable to the type of analysis set forth *in re Kerkhoven*, 205 USPQ 1069 (CCPA 1980) wherein the court held that it is prima facie obvious to combine two compositions that is taught by the prior art to be useful for the same purpose in order for a third composition that is to be used for the very same purpose since the idea of combining them flows logically from their having been individually taught in the prior art. Applying the same logic to the instant process claims, one of ordinary skill in the art would have had reasonable expectation of success that by administering an effective dose of adenosine receptor antagonist taught by Diamond et al in combination with an effective dose of dopamine receptor antagonist taught by Beasley et al, one would achieve a method of treating one or more symptoms associated with chronic consumption of a substance abuse.

As to the limitation "wherein the effective amount of adenosine receptor antagonist is lower than the effective amount of an adenosine receptor antagonist...." of claim 1 and 146, it is the purview of one skilled in the art to reduce the amount of active agents when combining two agents to reduce side affect and toxicity and improve patient compliance.

With respect to claims 149, 150, 152, 153, even though the references are silent as to administration of a standard, sub-threshold, and a threshold dosage, It would

have been prima facie obvious to one of ordinary skill in the art to combine the teaching of Diamond and Beasley to optimize via routine experimentation the dosage range recited in Diamond and Beasley because Diamond suggests the amount PD115199 depends on the subject being treated, the severity and nature of the affliction, the manner of administration, the potency and pharmacodynamics of the particular agent and Beasley suggests a lower dose than the standard dose for the treatment of alcohol, thus resulting in the practice of the instantly claimed invention.

MPEP 2144.5(A) states:

Optimization Within Prior Art Conditions or Through Routine Experimentation

> Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)

One would have been motivated to do so; with reasonable expectation of success because such optimization is routine in the pharmaceutical and would have been readily accomplished by one of ordinary skill in the art without undue burden. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

With respect to claims 156, 157, 159, 160, one would have recognized lowering the dosage of these agents would reduce the side effects caused by these agents. The side effects recited in these claims are well known because these compounds are well known in the art and efficacy and toxicity have already been proven. These minor

differences found adverse symptoms does not render the claims patentable distinct because the techniques and skills for determining efficacy and toxicity are well within the level of the ordinary skilled artisan and commonly practiced in the state of the art, and thus absent evidence to the contrary.

Applicant argues that the cited references alone or in combination do not disclose all the limitation of claim 1 and since none of the references disclose administering both adenosine receptor antagonist and dopamine receptor antagonist, it is impossible for the references to teach the therapeutically effective amount of the adenosine receptor antagonist is lower than the therapeutically effective amount of adenosine receptor antagonist administered without said dopamine receptor antagonist. In response, the language "therapeutically effective amount of the adenosine receptor antagonist is lower than the therapeutically effective amount of adenosine receptor antagonist administered without said dopamine receptor antagonist" is not clear how an effective amount of adenosine receptor antagonist is lower than a therapeutically effective amount of the same receptor antagonist. Accordingly, if the language is intended to mean therapeutically effective amount of the adenosine receptor antagonist is lower than the reference therapeutically effective amount of adenosine receptor antagonist (normal routine dose) administered without said dopamine receptor antagonist, the new rejection still applies as it is routine practice in the art to lower dosage of active agents when combining them to reduce side affect and toxicity and improve patient compliance. Additionally, Applicant argues that Koch teaches away

from the claimed invention, In response, Fink and Koch are no longer cited in the new rejection above so therefore this argument pertaining to these references are not longer applicable.

New Rejection necessitated by claim amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 146, 148-153, 155-166 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is necessitated by the claim amendment.

The language "therapeutically effective amount of the adenosine receptor antagonist is lower than the therapeutically effective amount of adenosine receptor antagonist administered without said dopamine receptor antagonist" is not clear how an effective amount of adenosine receptor antagonist is lower than a therapeutically effective amount of the same receptor antagonist. Accordingly, if the language is intended to mean therapeutically effective amount of the adenosine receptor antagonist is lower than some unstated reference therapeutically effective amount of adenosine receptor antagonist (e.g., some normal routine dose) administered without said dopamine receptor antagonist, the new 103 rejection above still applies.

Claim 1 recites the limitation “said therapeutically effective amounts", twice in lines 7-8. There is insufficient antecedent basis for these limitations in the claim.

It is also noted that there are two “said therapeutically effective amounts", that appear to be different values, based on applicants arguments. However, only one of these has antecedent basis; therefore, at least one of the “said therapeutically effective amounts” of claim 1, lines 7-8 also lacks antecedent basis.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JEAN CORNET whose telephone number is (571)270-7669. The examiner can normally be reached on Monday-Thursday 7.00am-5.30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on 571-272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JC/

/Timothy P Thomas/
Primary Examiner, Art Unit 1628